UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,682	10/29/2003	Xing Su	21058/1206739-US1	9817

7278 7590 10/01/2007

DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER
HA, JULIE

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
10/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/697,682	SU ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *17-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☒ Claim(s) *2-3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restriction filed on July 24, 2007 is acknowledged. Claims 1-30 are pending in this application.

Julie Ha is the Examiner of Record.

Restriction

1. Applicant's election of Group I (Claims 1-16), drawn to a method of identifying a protein based on distance maps, in the reply filed on July 24, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Restriction requirements are deemed proper and made FINAL.

2. Claims 17-30 are withdrawn from further consideration, pursuant to 37 CFR 1.142(b), as being drawn to nonelected Inventions, there being no allowable generic or linking claim. Claims 1-16 are examined on the merits in this office action.

Objection-Claims

3. Claims 2-3 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 2 recites a method of claim 1, further comprising a) placing a template nucleic acid into at least one chamber, each chamber to contain a different type of amino acid, and b) producing one

or more labeled proteins, polypeptide or peptides encoded by the template nucleic acid. Claim 3 recites the method of claim 1, further comprising: a) obtaining one or more proteins, polypeptides or peptides from a biological sample; and b) labeling the proteins, polypeptides or peptides post-translationally. However, claim 1 recites a method comprising a) obtaining one or more labeled proteins, polypeptides or peptides. Claims 2 and 3 do not further limit claim 1; claims 2 and 3 are required to occur prior to claim 1, since claim 1 requires labeled proteins, polypeptides or peptides, and claims 2 and 3 recite method of labeling proteins, polypeptide or peptides.

Rejection-35 U.S.C. 112, 2nd

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 2 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 2 recites the limitation "template nucleic acid into at least one chamber" in line 1 of claim 2. There is insufficient antecedent basis for this limitation in the claim. The template nucleic acid and chamber is never mentioned in claim 1. The first time template nucleic acid and chamber appear is in claim 2. Claim 1 is drawn to a method of obtaining one or more labeled peptide.

7. Claim 9 recites "the method of claim 2, wherein the labeled amino acids in each chamber represent between about 0.5% and about 50% of the total amount of the same

amino acid in that chamber." The phrase "about 0.5% and 50% of the total amount of the same amino acid in that chamber" is unclear. It is unclear what "total amount of the same amino acid in that chamber" is referring to. Claim 2a recites "placing a template nucleic acid into at least one chamber, each chamber to contain a different type of labeled amino acid". According to claim 2a, different type of labeled amino acid is in each chamber. Thus, when claim 9 recites "labeled amino acids in each chamber represents about 0.5% and 50% of the total amount of the same amino acid in that chamber" it is unclear what other amino acids are present in each chamber. Each chamber should only contain one labeled amino acid.

Rejection-35 U.S.C. 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 4-5, 7-8, 10-14 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Chan EY (US Patent # 6210896).

10. The instant claims are drawn to a method comprising a) obtaining one or more labeled proteins, polypeptides or peptides, b) passing the labeled proteins, polypeptides or peptides through one or more nanopores, c) detecting labeled amino acid residues in the labeled proteins, polypeptides or peptides, d) compiling an amino acid distance map

for each type of labeled amino acid, and 3) identifying the protein based on the distance maps. The claims are further drawn to the method wherein the protein, polypeptide or peptide is identified by comparing the distance maps with a library of amino acid distance maps, identified by comparing the distance maps with sequences of known proteins. Furthermore, the claims are drawn to wherein each nanopore is operably coupled to a detector, and wherein only one labeled protein, polypeptide or peptide passes through a nanopore at a time, and the time between passage of a first labeled amino acid through the nanopore and passage of a second labeled amino acid through the nanopore corresponds to the distance along the labeled protein, polypeptide or peptide between the first and second amino acids, and the labels are selected from the group consisting of luminescent labels, fluorescent labels, phosphorescent labels, chemiluminescent labels...nuclear magnetic resonance labels...electron spin resonance labels...and are detected with a photodetector or with an electrical detector.

11. Chan EY teaches methods and products for analyzing polymers, and the use of molecular motors to move polymers with respect to a station such that specific signals arise from the interaction between the polymer and an agent at the station (see abstract). The reference teaches the method for analyzing polymers based on the ability to examine each unit of a polymer individually, and by examining each unit individually the type of unit and the position of the unit on the backbone of the polymer can be identified (see column 2, lines 32-38). Furthermore, the reference teaches that one aspect of linear analysis techniques involves the movement of the polymer past a station in such a manner as to cause a signal that provides information about the

polymer to rise (see column 2, lines 52-55). Furthermore, the reference teaches that a method for analyzing a polymer includes the steps of exposing a plurality of individual units of a polymer to an agent selected from the group consisting of an electromagnetic radiation source, a quenching source, and a fluorescence excitation source causing the molecular motor to move the polymer relative to the agent, and detecting signals resulting from an interaction between the units of the polymer and the agent (see column 2, lines 60-67 and column 26). Furthermore, the reference discloses that another preferred method of analysis involves the use of radioactively labeled polymers (see column 27, lines 9-10) and the analysis of the radiolabeled polymers is identical to other means of generating signals (see column 27, lines 47-48). The reference teaches that in one embodiment, the polymer dependent impulses measured is an electromagnetic radiation signal generated, and the units are detected at the signal generation station by measuring light emission at the station, the station can be a nanochannel (see column 6, lines 5-9). The reference further teaches a method for determining the order of units of a polymer of linked units, the method steps includes 1) moving the polymer linearly relative to a station using a molecular motor, 2) measuring a polymer dependent impulse generated as each of two individual units, each giving rise to a characteristic signal, pass by the station, 3) repeat steps 1 and 2, and 4) determining the order of at least the two individual units based upon the information obtained from said plurality of similar polymer (see column 5, lines 54-63). The reference further teaches that the polymer may be any type of polymer of linked units...nucleic acid or peptide (see column 3, lines 27-32). This reads on claims 1, 5, 7-

8, 11-14. The reference further teaches that the labeled polymer is moved linearly relative to a station to produce a characteristic polymer dependent impulse generated as each of the two unit labels passes by the station, and further comprising the step of determining the distance between the polymer dependent impulses as an indication of the distance between the two unit labels (see column 4, lines 35-41). This reads on claims 1, 4, 7-8 and 16. Furthermore, the reference teaches that the method is a method for determining the proximity of two unit labels of the polymer wherein the proximity of the two unit labels is the signature of said polymer dependent impulses, the identity of each unit label being indicative of the identity of at least one unit of the polymer, wherein the labeled polymer is moved relative to a station to expose the two unit labels to the station to expose the two unit labels to the station to produce a characteristic polymer dependent impulse arising from a detectable physical change in the unit label or the station, and further comprising the step of measuring the amount of time elapsed between detecting each characteristic polymer dependent impulse, the amount of time elapsed being indicative of the proximity of the two unit labels (see column 4, lines 42-54). This reads on claim 10. The reference discloses that sequence of polypeptide is determined by comparing the relative mass difference between fragments with the known masses of the amino acid residues (see column 2, lines 8-21). This reads on claim 4. Furthermore, the reference discloses that the ability to determine the distance between two units is important for determining how many units, if any, are between the two units of interest and the sequence of units serves as a blueprint for a known polymer (see column 13, lines 25-32). Furthermore, the reference

discloses analysis of labeled peptide analyzed by nanochannel FRET sequencing. The sequence-specific FRET information arising from each fragment is sorted into one of two complementary strand groups, sorting allows population analysis to determine the positions of all the desired bases, and to thus generate sequence information from the sorted data (see column 21, lines 19-26). Therefore, the reference meets the limitations of claims 1, 4-5, 7-8, 10-14 and 16.

Rejection-35 U.S.C. 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chan EY (US Patent # 6210896) as applied to claims 1, 4-5, 7-8, 10-14 and 16 above.

16. The instant claim is drawn to a method comprising a) obtaining one or more labeled proteins, polypeptides or peptides, b) passing the labeled proteins, polypeptides or peptides through one or more nanopores, c) detecting labeled amino acid residues in the labeled proteins, polypeptides or peptides, d) compiling an amino acid distance map for each type of labeled amino acid, and 3) identifying the protein based on the distance maps and obtaining one or more proteins, polypeptides or peptides from a biological sample, and labeling the proteins, polypeptide or peptides post-translationally.

17. The teachings of Chan EY are described supra. The difference between the reference and the instant application is that the reference does not teach obtaining one or more proteins, polypeptides or peptides from a biological sample.

18. However, it would have been obvious to one of ordinary skill in the art to try the method of obtaining the identity of the protein of any sample, including proteins from biological samples, by using the teachings of US Patent '896. There is a reasonable expectation of success since the method and the analysis of the Chan patent works on

any polymeric compounds, such as DNA, RNA, and proteins that are labeled with luminescent labels, fluorescent labels, phosphorescent labels, chemiluminescent labels...nuclear magnetic resonance labels...electron spin resonance labels...and are detected with a photodetector or with an electrical detector.

19. Claim 2, 6, 9 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan EY (US Patent # 6210896) as applied to claims 1, 4-5, 7-8, 10-14 and 16 above in view of Thompson et al (US Patent # 5324637).

20. The instant claims are drawn to the method of claim 1, further comprising: a) placing a template nucleic acid into at least one chamber, each chamber to contain a different type of labeled amino acid, and b) producing one or more labeled proteins, polypeptides or peptides encoded by the template nucleic acid, and wherein each chamber is operably coupled to a different set of nanopores, and wherein the labeled amino acids in each chamber represent between about 0.5% and about 50% of the total amount of the same amino acid in that chamber.

21. The teachings of Chan EY are described supra. The difference between the reference and the instant claims are that the reference does not teach nucleic acid into at least one chamber, each chamber containing a different type of labeled amino acid, and producing one or more labeled proteins, polypeptides or peptides encoded by the template nucleic acid, and the amount of labeled amino acid present in each chamber.

22. However, Thompson et al teaches a method for coupling transcription and translation from DNA, wherein RNA is transcribed from DNA and RNA translates into

protein (see abstract). The reference further teaches that if a radiolabeled amino acid is used in the coupled reaction, such as ^{35}S methionine or ^{3}H leucine, then the corresponding amino acid is left out of the amino acid mix...RNA polymerase, either SP6, T7 or T3 is then added (see column 8. lines 60-65). Furthermore, the reference teaches that another method of measuring the amount of protein produced in coupled in vitro transcription and translation reactions is to perform the reactions using a known quantity of radiolabeled amino acid such as ^{35}S methionine or ^{3}H leucine and subsequently measuring the amount of radiolabeled amino acid incorporated into the newly translated protein (see column 11, lines 40-46).

23. Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Chan EY patent and Thompson et al patent to obtain the protein identity, because both prior arts teach the identification of proteins, using labeling of the protein such as fluorescence labeling, radiolabeling of proteins (Chan) and radiolabeling of proteins (Thompson) to quantify and identify the proteins. There is a reasonable expectation of success, since Thompson et al provide a simple method for producing protein from a template DNA, such a method which can be used to couple transcription and translation of a single protein coded by the DNA template (see Thompson et al, column 4, lines 13-20). Furthermore, both prior arts teach radiolabeling of proteins to measure the amounts of labeling and Chan teaches limiting the region of detection of the polymer where the radiolabel exists on the protein.

24. It has been held that under KSR that “obvious to try” may be an appropriate test under 103. The Supreme Court stated in KSR, When there is motivation “to solve a

problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727,_,82 USPQ2d 1385, 1397 (2007).

25. The "problem" facing those in the art was that sequencing polymer methods are slow and labor intensive. For example, Sanger method involves the enzymatic synthesis of DNA molecules terminating in dideoxynucleotides, and subsequent analysis yields information of the length of the DNA molecules and the nucleotide at which each molecule terminates, and thus, the DNA sequence can be determined. The other method is Maxam and Gilbert method, which uses chemical degradation to generate a population of molecules degraded at certain positions of the target DNA, and with knowledge of the cleavage specificities of the chemical reactions and the lengths of the fragments, the NDA sequence is generated (see Chan patent '896, column 1, lines 32-47) and each process takes about 1-3 days, and there were a limited number of methodologies available to do so, for example radiolabeling the protein sequence, DNA sequencing, mass spectroscopy and ELIDA sequencing. The skilled artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful. In this case, Chan patent teaches that any polymer sequence can be labeled and run through the nanochannel, and the distance of each polymeric sequence can be read separately, for any DNA and protein sequences. Thus,

performing a transcription coupled translation a radiolabeling the protein that is translated from RNA is a "the product not of innovation but of ordinary skill and common sense," leading to the conclusion that invention is not patentable as it would have been obvious.

Conclusion

26. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Julie Ha
Patent Examiner
AU 1654

ASHISH GUPTA
PRIMARY EXAMINER